

# MATRIX:

Developing the next generation of  
HIV prevention products for women

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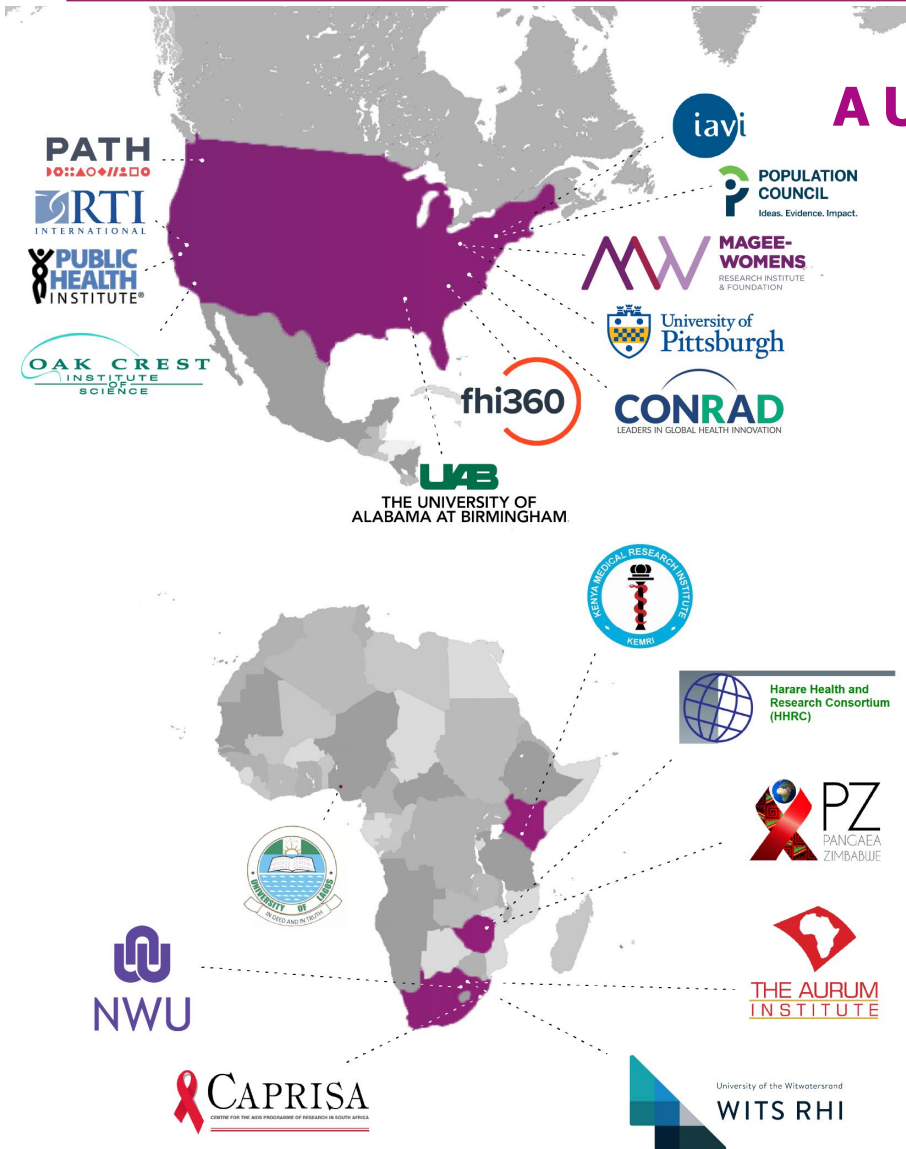


# What is MATRIX?

## A USAID Project to Advance the Research and Development of Innovative HIV Prevention Products for Women

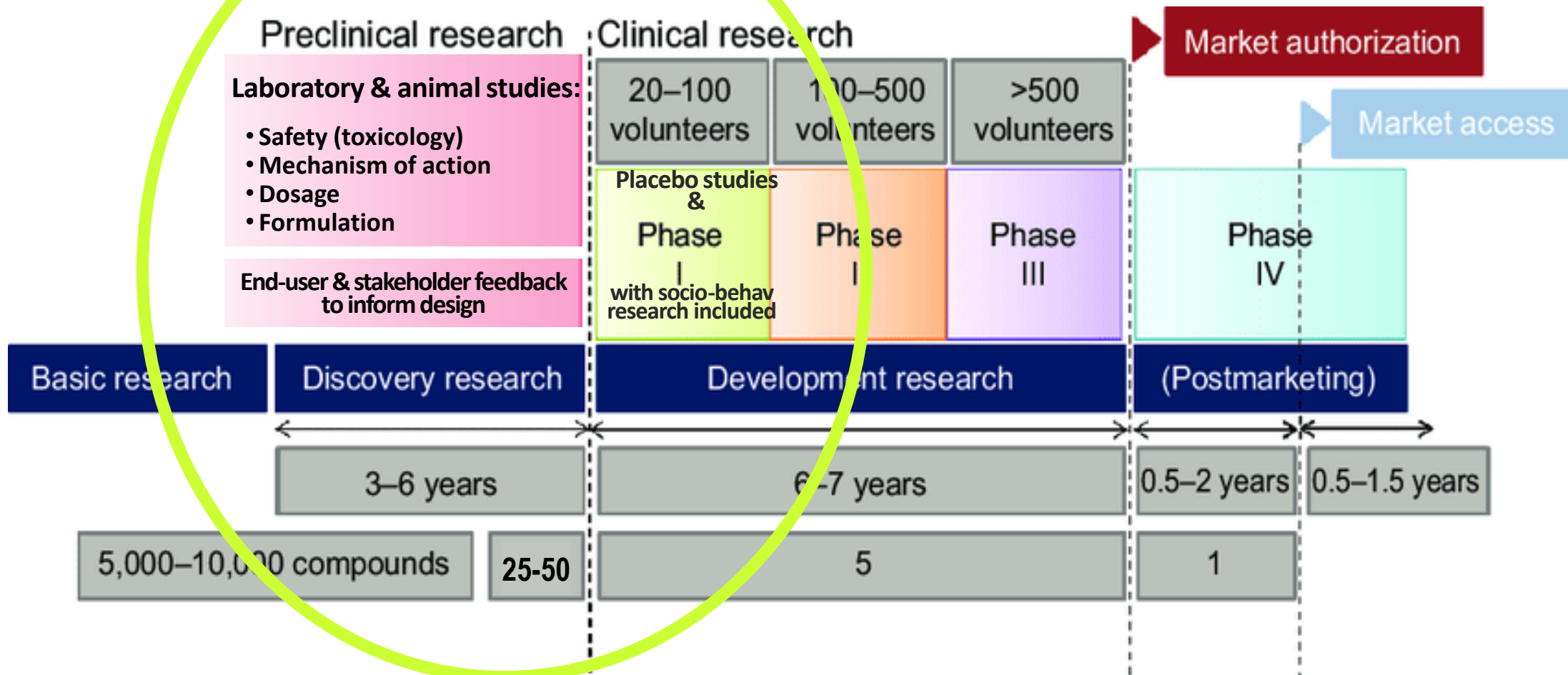
- 5-year \$125M Cooperative Agreement (2021-2026)
- Being implemented by Magee-Womens Research Institute and Foundation (MWRIF) with 17 partners in South Africa, Kenya, Zimbabwe, US
- Brings together expertise in product development, clinical trials, social and behavioral research, and market and business case development

**Project Goal:** Through North-South partnerships, to develop a range of HIV and dual-prevention products that in addition to being safe and effective are *acceptable, affordable, scalable* and *deliverable* to fulfill the unmet needs of women at risk of HIV infection and unplanned pregnancy.



# MATRIX focuses mostly on *early* R&D of products

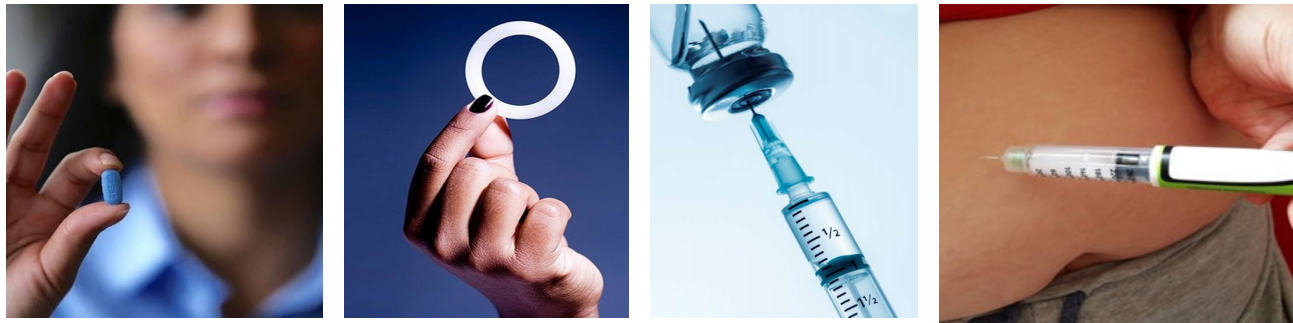
Most of our products have not yet been evaluated in a Phase 1 clinical trial



# Do we need more HIV prevention methods?

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Although the HIV prevention landscape has changed (with more choices and higher efficacy!) the short answer is **YES!**



- There is no “magic bullet” for HIV prevention; high efficacy is only one consideration when making a choice
- Looking ahead, almost all products in late-phase clinical trials are systemic, and most are long-acting
- Providing options that allows people to make choices for what will work best in the context of their lives is vitally important

# Looking to the future with a range of products

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- We aim to develop a **range of prevention products** to ensure women have more options:
  - **Dual-purpose** products for prevention of both HIV and pregnancy
  - **On-demand short-acting** vaginal products meant to be used around the time of sex
  - Vaginal **non-systemic** products to be used for a **month** at a time
  - **Ultra long-acting** products providing protection for a year or longer
- Some are new formulations of existing ARV-based products; others contain novel agents

# The realities of product development

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- It's a long and complex process that can take 10-15 years for a candidate to make its way from laboratory research to regulatory approval
- **The odds of success are slim**
  - Of 10,000 compounds at the discovery stage, perhaps 1 will be approved
  - Only 1 in 10 drug candidates in clinical trials will likely be approved
- **"Failure" can happen at any point and for any number of reasons**
  - Found not to be safe
  - Poor adherence – it's not a product women are likely to use
  - Too costly to manufacture or impractical to deliver
  - Doesn't add value

# How we might improve the odds for success

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- **End-user preferences** and **cost & feasibility** are considered *early* in the process
- Conducting **Placebo studies** and **Phase 1 trials in Africa** – in parallel with US – to obtain safety and acceptability data in the intended populations of women, *from the start*
- A **nimble** and **responsive approach** and milestone- and benchmark-driven process with clearly defined **“Go/No-Go” criteria**.
- An independent **scientific advisory group** (SAG) provides unbiased **assessment of a product’s progress** in meeting timelines and milestones – makes recommendations to USAID

**It’s not enough that laboratory and animal studies suggest the product will be safe and effective in humans.**

**There must also be likelihood/evidence that:**

- ✓ **End-users will use the product**
- ✓ **It can be manufactured and distributed locally and at low cost**
- ✓ **It will be easy to deliver, with minimal burden on healthcare systems**
- ✓ **It will meet the needs of Ministries of Health and national prevention programs**
- ✓ **It can provide added value**

# An ongoing bidirectional process to inform and expedite the research and development of products





# Enabling capacity strengthening in the Global South

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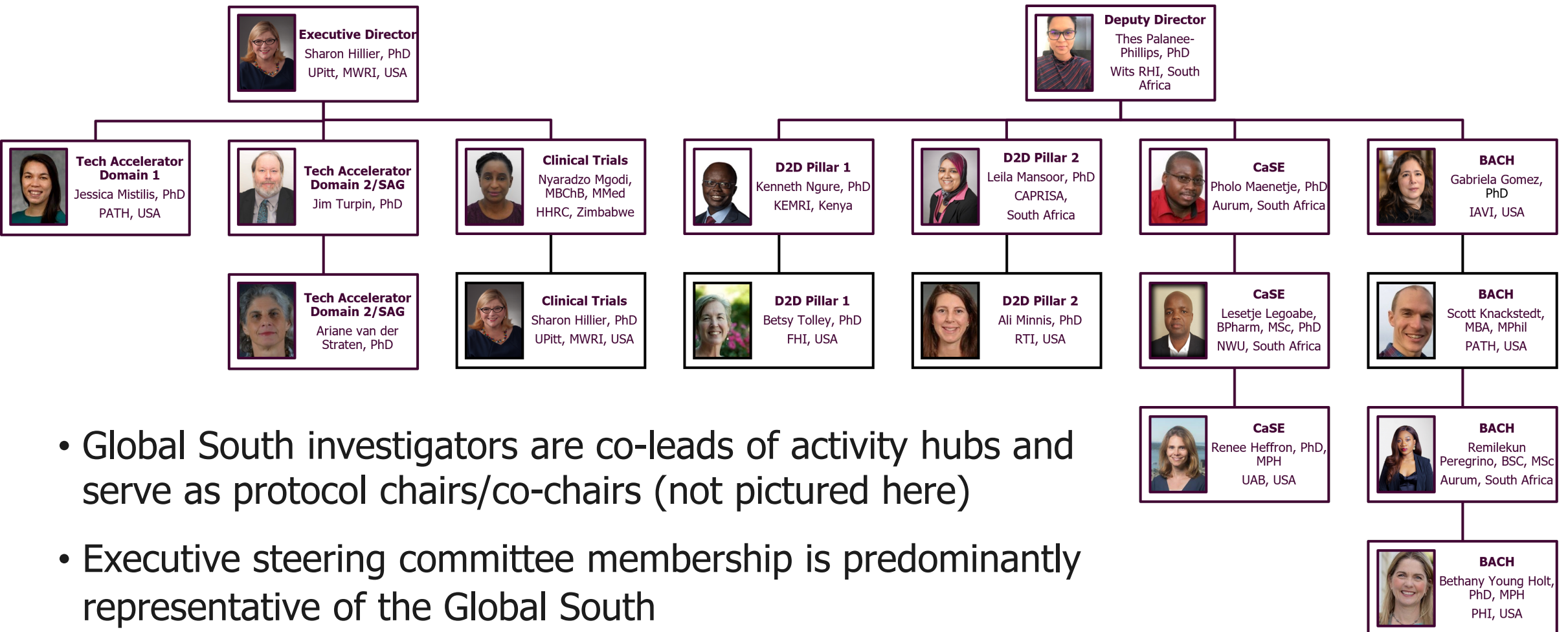
- MATRIX aims to **develop a range of prevention products** for women through a unique R&D process
- MATRIX also aims to **facilitate full and sustainable ownership** of this work by the Global South into the future through:



- A structure of balanced **North-South partnerships**
- Mechanisms for **strengthening the R&D capacity** of African investigators and infrastructures

# Sharing power is the first step to shifting power

## MATRIX Leadership: Global South researchers are equal partners



- Global South investigators are co-leads of activity hubs and serve as protocol chairs/co-chairs (not pictured here)
- Executive steering committee membership is predominantly representative of the Global South

# Strengthening R&D capacity: Early phase trials being conducted in Africa

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- Africa represents 18% of the world's population and carries 25% of the global disease burden, yet less than 3% of early phase clinical trials take place in Africa.
- In MATRIX, **early phase** and **first-in-human studies are taking place in the Global South** (and the US).
  - Allows us to collect **data in the product's intended populations of women**
  - Enables **African investigators** and **trial site teams to gain experience** in the conduct of these complex studies
  - Supports **capacity strengthening** of **regulatory authorities** and **ethics committees** in review and oversight of early phase trials

# Strengthening R&D capacity: Fellowships and learning opportunities

## Building and growing the Next Generation of HIV Prevention Researchers

- Providing skills development and growth for early- and mid-career African researchers through fellowships, mentorship and learning opportunities
- From e-learning courses to 6-18-month scholarships
- Topics include early product development, biostatistics, socio-behavioural research, business case modeling

- **Njeri Wairimu** is a social scientist at KEMRI's Thika Project who took part in a **1-year scholarship providing training and mentorship in human-centered design.**
- She worked with the MATRIX team looking to understand the needs and preferences of potential end-users (D2D Pillar 1) and was mentored by **Prof. Kenneth Ngure**, co-lead of D2D Pillar 1
- Njeri continues to learn and grow as member of the D2D Pillar1 team.



**“My experience ... expanded my knowledge and creativity in conducting research. I have a new appreciation of study participants as collaborators in research ...”**

# Strengthening R&D capacity: Funding promising African researchers and projects

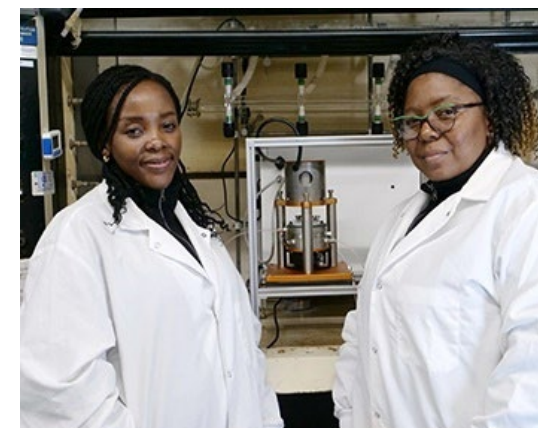
- 100% of active pharmaceutical ingredients (APIs) needed to formulate ARVs and PrEP for use in Africa are imported – and at great cost.
- MATRIX Independent Special Project: **Development of the spin synthesis process for tech transfer & cost-effective manufacturing of APIs in Africa** – is evaluating innovative continuous flow technology

**By funding seed grants and independent special projects, MATRIX is supporting programs that will add value and strengthen the capacity of ongoing R&D in the Global South.**



**KinetiChem's Synthetron reactor system** (photo credit -KinetiChem)


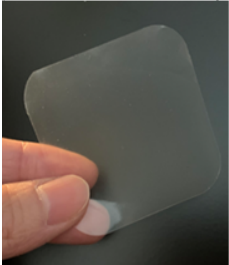

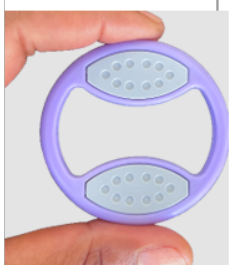
- Being led by Kelly Chibale & Susan Winks (H3D Foundation and University of Cape Town-UCT)
- A collaboration between **Holistic Drug Discovery & Development Centre at UCT** (H3D, South Africa), **Oak Crest Institute of Science** (USA), **CPT Pharma** (South Africa) & **KinetiChem** (USA)
- Two post-doctoral fellows trained at Oakcrest, US



**Thembele Sonti and Kanyisile Mhlana** (UCT post-docs) while at Oak Crest Institute of Science

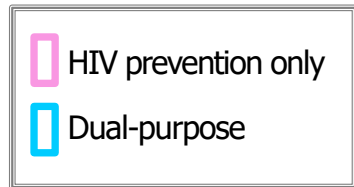
# MATRIX's Products and Studies

# MATRIX current product pipeline

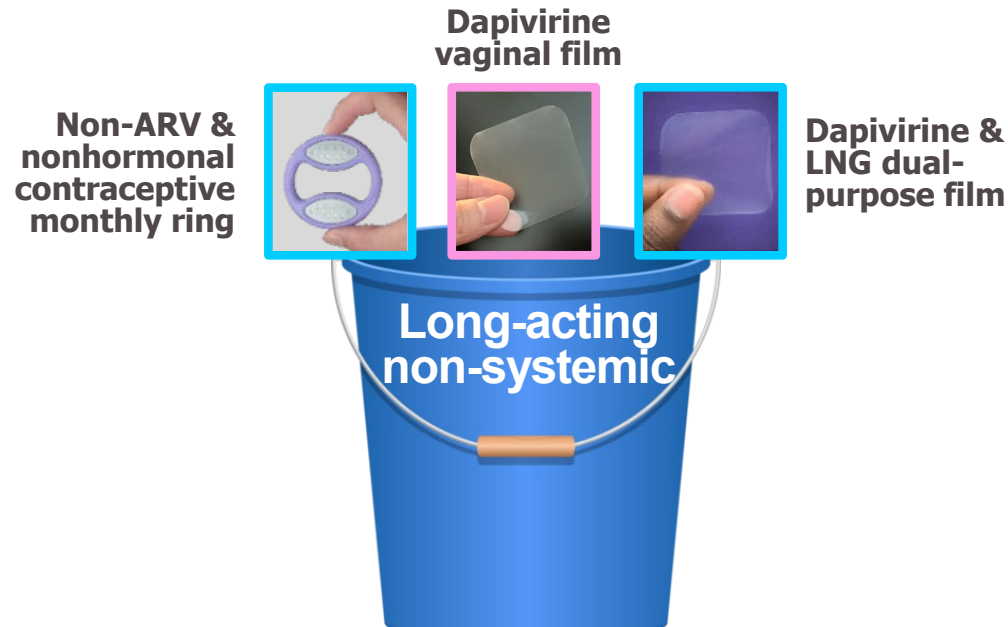
Product	Developer	Product Type	Active Ingredient(s)	How used	Protection Goal	Unique Features/ Additional Info	Development Status
 <p><b>TAF/EVG Fast-dissolving vaginal insert</b></p>	<b>CONRAD</b> (USA)	<b>Fast-dissolving insert</b>	<b>TAF/EVG</b> <i>tenofovir alafenamide &amp; elvitegravir</i> <i>NRTI &amp; integrase inhibitor (ARVs)</i>	<b>On-demand</b> <i>(women insert themselves at time of sex)</i>	<b>At least 1 day</b>	TAF shows activity against HSV- may be added benefit. . Outside of MATRIX, CONRAD evaluating as rectal insert.	<b>MATRIX-001</b> – safety and acceptability Phase 1 study (US & African sites)..
 <p><b>Dapivirine vaginal film</b></p>	<b>Univ of Pittsburgh</b> (USA)	<b>Vaginal film</b>	<b>Dapivirine</b> <i>NNRTI (ARV)</i>	<b>Women insert themselves</b>	<b>1 month</b>	Film would slowly release drug as it dissolves. <i>Also being developed as dual-purpose</i>	<b>MATRIX-002</b> – safety, acceptability & usability of 2 placebo films (US & African sites) –informing film design for first-in-human trial of active product.
 <p><b>Dapivirine &amp; levonorgestrel dual-purpose vaginal film</b></p>	<b>Univ of Pittsburgh</b> (USA)	<b>Vaginal film</b> <i>(dual purpose)</i>	<b>Dapivirine</b> <i>NNRTI (ARV)</i> <b>Levonorgestrel (LNG)</b> <i>(hormonal contraceptive)</i>	<b>Women insert themselves</b>	<b>1 month</b>	Film would slowly release dapivirine and LNG as it dissolves	<b>Pre-clinical</b>
 <p><b>Non-ARV/ nonhormonal contraceptive dual-purpose vaginal ring</b></p>	<b>Oak Crest Inst of Science</b> (USA)	<b>Vaginal ring</b> <i>(dual purpose)</i>	<b>Antiviral peptide</b> <i>(protein fragmen -non-ARV)</i> <b>soluble Adenylyl Cyclase (sAC) inhibitor</b> <i>(non-hormonal contraceptive)</i>	<b>Women insert themselves</b>	<b>1 month</b>	Antiviral shows activity against HSV & HPV- may be added benefit. sAC inhibitor affects sperm's ability to swim	<b>MATRIX-003</b> – acceptability of 2 placebo rings (US & African sites) – deciding ring for first-in-human study of active product.

# Prioritizing the most impactful biomedical HIV prevention products

MATRIX aims to develop a range of **HIV prevention products** for women, including **dual-purpose products**, in order to meet the diverse needs of women, with at least **one promising product in each category** advancing down the development pathway



**Short-acting, on-demand**  
vaginal products used around the time of sex



**Long-acting non-systemic**  
vaginal products to protect for **1 month or longer**



**Ultra long-acting**  
products to protect for **1 year or longer**



# MATRIX studies at a glance



## **MATRIX-001**

- **Phase 1 study** of safety, drug distribution and acceptability of **TAF/EVG fast-dissolving insert**
- First Phase 1 in African women
- 3 sites: **Kenya**, South Africa, US
- Enrollment of 60 participants near complete
- Results expected 2025

## **MATRIX-004**

- **Phase 1 trial in development**



## **MATRIX-002**

- **Placebo study** of 2 prototype monthly vaginal films for acceptability, usability and safety
- To inform film design for first-in-human trial of **monthly dapivirine film**
- 5 sites: **Kenya**, South Africa (2), US, Zimbabwe
- Enrollment of 100 participants near complete
- Results expected Q4 2024/Q1 2025

## **MATRIX-006**

- To be developed



## **MATRIX-003**

- **Placebo study** of 2 prototype rings for safety and acceptability.
- To inform ring design for Phase 1 trials related to **non-ARV / nonhormonal contraceptive monthly dual-purpose vaginal ring**
- 5 sites: South Africa (3), US, Zimbabwe
- To enroll 100 participants
- Results expected 2025

## **MATRIX-005**

- Beginning to develop

# MATRIX-007 (CARE-PrEP) study



- Will enroll up to 800 participants in the CATALYST implementation study who become pregnant and opt to continue use of ARV-based prevention, as well as their infants
- **Aims to contribute quality data** on the **safety** of **CAB-LA, dapivirine ring and oral PrEP during pregnancy** – data on the use of CAB-LA is especially important
- To be conducted at sites in **Kenya, Lesotho** and **Zimbabwe**.
- Pending ethics and regulatory approvals, expect to begin screening and enrollment Oct 2024
- Study is expected to be completed 2026

MATRIX is collaborating with the USAID-funded MOSAIC collaborative, drawing on the experience and expertise in this specialized area of research of team members from both programs, most notably as part of the NIH-funded Microbicide Trials Network

# Change is the only constant!

## It's a new, exciting – and still evolving – landscape!

- The HIV prevention landscape is changing – with new products and higher efficacy – and the context in which we work is also changing:
  - There's a desire to see that **product development** and **manufacturing** can take place **in Africa**
  - Harmonization and reliance have been the pillars for **capacity building** of **national regulatory authorities** and in the establishment of the **African Medicines Agency**
- MATRIX must keep pace with the current and evolving context and structures – and be attentive to the needs of the countries and communities within which we work



# MATRIX: Stakeholder Engagement



- This is MATRIX's second stakeholder meeting in Kenya – the first was in Nov 2022
- That meeting was larger and more diverse, serving mostly to introduce MATRIX and seek feedback on our products pipeline, particularly from young women.
- Today's meeting is focused more on:
  - Seeking your feedback on **key questions** regarding development of our **current products**, including **dual-purpose products**, with respect to **regulatory pathways, cost, manufacturing** and **delivery**
  - Understanding the **needs and priorities** of **Kenya's strategic framework** for HIV prevention and **how best MATRIX can align** with these



# MATRIX: Developing a range of HIV prevention options for women for use at different times in their lives



- **Dual-purpose** products for preventing both HIV and pregnancy
- **On-demand** products
- **Monthly non-systemic** products
- **Ultra long-acting** products for 12 months

- ✓ **Efficacy**
- ✓ **Safety**
- ✓ **Ease of use**
- ✓ **Discretion**
- ✓ **Price**
- ✓ **Availability**
- ✓ **Accessibility**

# Acknowledgements

# MATRIX

Advancing R&D of Innovative  
HIV Prevention Products for Women

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*The contents in this presentation are those of the presenter and do not necessarily reflect the view of the U.S. President's Emergency Plan for AIDS Relief, the U.S. Agency for International Development or the U.S. Government.*

